

IMGT/3Dstructure-DB and tools for immunoglobulins (IG) or antibodies, T cell receptors (TR), MHC, IgSF and MhcSF structural data

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<http://www.imgt.org>

IMGT®, the international ImMunoGeneTics information system®, provides a three-dimensional (3D) structure database (IMGT/3Dstructure-DB) and tools for sequences and structures analysis (IMGT/DomainDisplay, IMGT/DomainGapAlign and IMGT/Collier-de-Perles). IMGT/3Dstructure-DB data are annotated according to the IMGT® criteria, using IMGT/DomainGapAlign, and based on the IMGT-ONTOLOGY concepts and axioms. IMGT/3Dstructure-DB provides IMGT gene and allele identification (CLASSIFICATION), region and domain delimitations (DESCRIPTION), amino acid positions according to the IMGT unique numbering (NUMEROTATION). Coupled to the IMGT/Collier-de-Perles tool, IMGT/3Dstructure-DB and IMGT/DomainGapAlign provide an invaluable help for antibody engineering and humanization design based on complementarity determining regions (CDR).

Ehrenmann F, Kaas Q. and Lefranc M.-P. Nucleic Acids Res 38: D301-307 (2010)

Kaas Q., Ruiz M. and Lefranc M.-P. Nucleic Acids Res. 32: D208-210 (2004)

Lefranc M.-P. et al Nucleic Acids Res. 37: 1006-1012 (2009)

Kaas Q., Ehrenmann F. and Lefranc M.-P. Brief. Funct. Genomic Proteomic, 6:253-264 (2007)

IMGT/DomainGapAlign

Amino acid sequences are analysed per domain using the IMGT/DomainGapAlign tool. Several sequences of the same domain type (V, C or G) may be analysed simultaneously.

Paste your protein sequence(s) in FASTA format below

```
+alemtuzumab_VH
QVLOESGPGLVRPSLTLCTVSGFTDFYMMWVPPGRIGLEIIFDIFRKAGKTYTEYNPSIKRVTILVDTSKNQFLRLSSVTVADATAYVYC
HTAAPPDYGQSLTVSSASTKGPSVFLAPSKSTGTAALGCLWDYFPEPVTVWSNSGALTSGVHTFPAVLQSSGLYSLSSVTVADATYVYC
QWVNPKNTRKDNVE
```

Sequence names must be different!

Upload a file

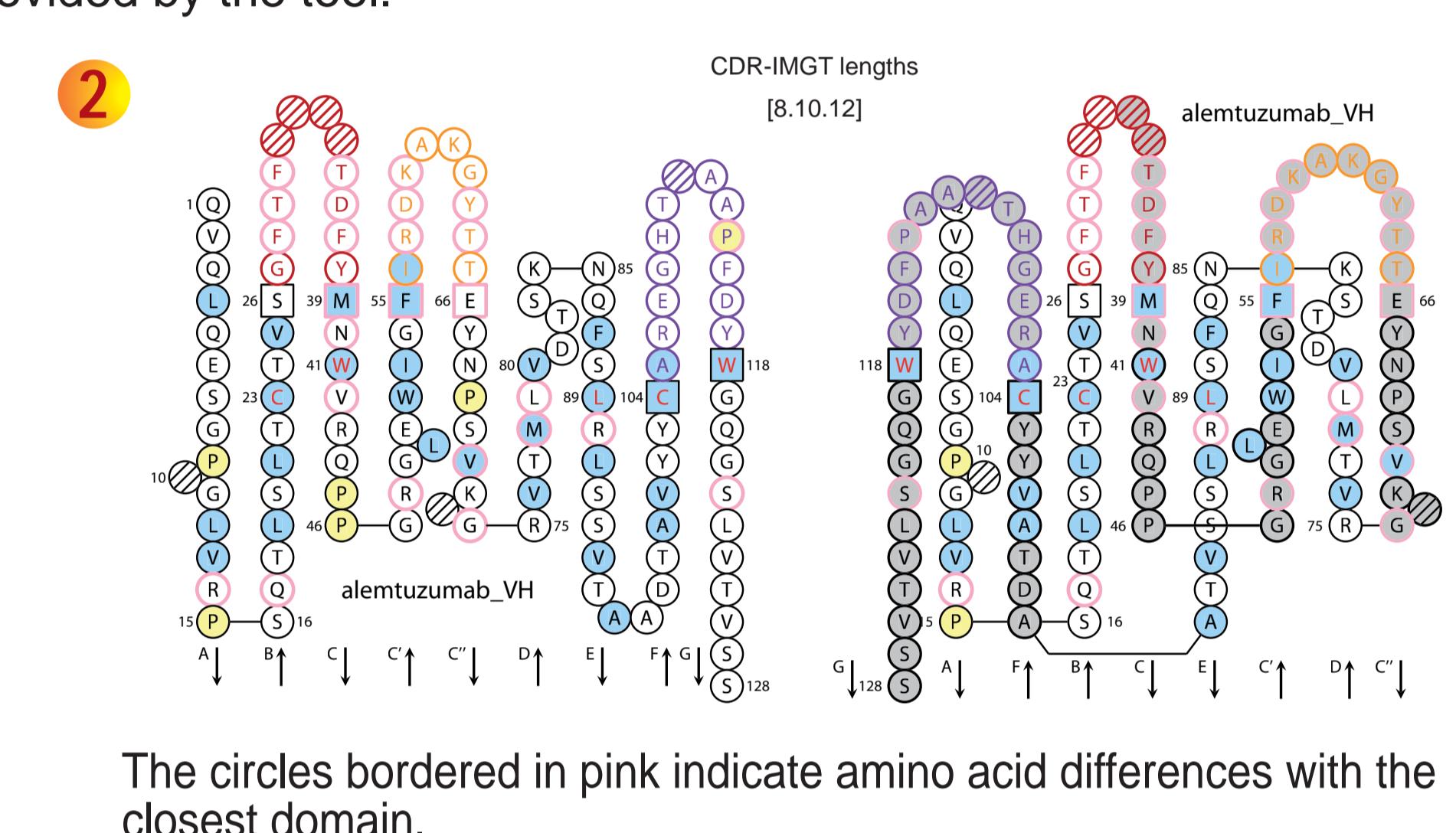
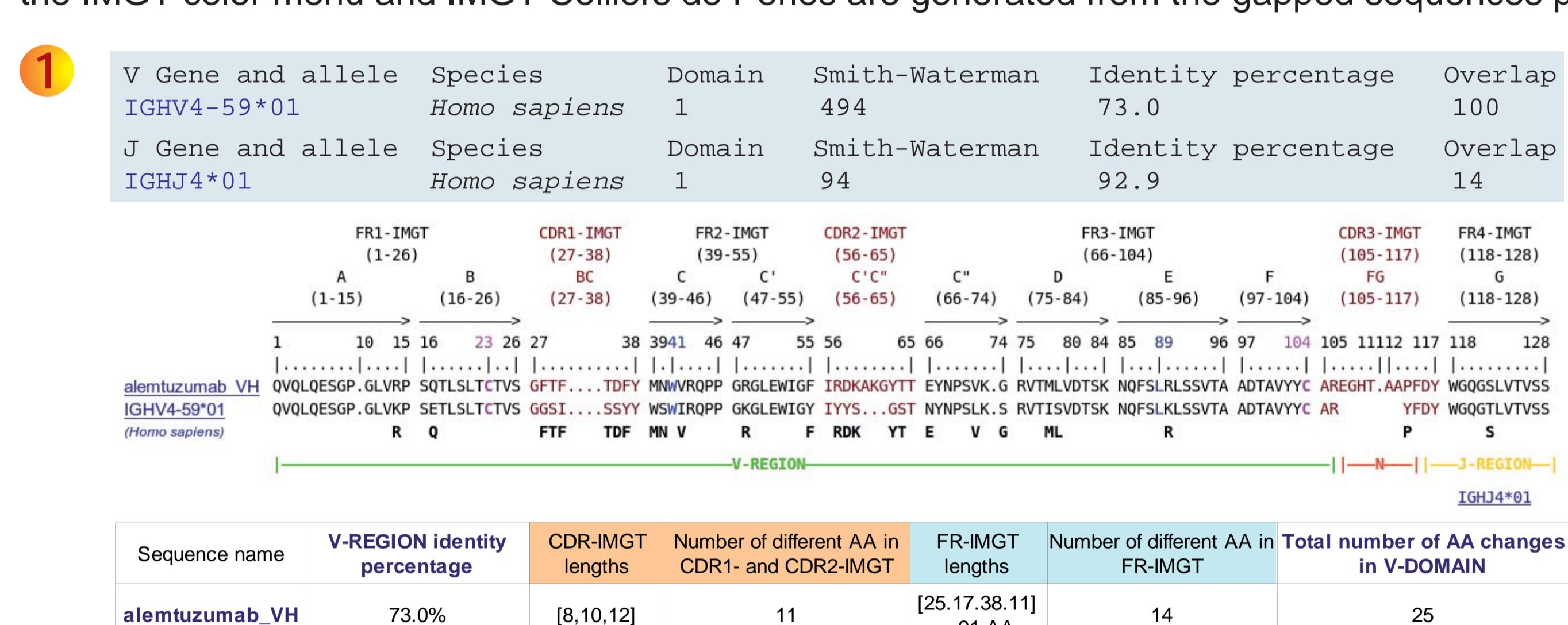
Select a domain type V

Select a species All species English name

Displayed alignments 1 Display IMGT Colliers de Perles

Align and IMGT-gap my sequence(s) Clear the form

IMGT/DomainGapAlign identifies the closest germline V-REGION (for 'V'), C-DOMAIN (for 'C') or G-DOMAIN (for 'G'), creates gaps according to the IMGT unique numbering and highlights differences with the closest reference(s). For an antibody V domain sequence, the tool identifies the closest germline V-REGION and J-REGION, and provides a delimitation of the strands, framework regions (FR-IMGT) and CDR-IMGT. The gene and allele name of the closest sequence(s) from the IMGT domain directory is provided with a percentage of identity and a Smith-Waterman score. Regions and domains are highlighted using the IMGT color menu and IMGT Colliers de Perles are generated from the gapped sequences provided by the tool.



IMGT/3Dstructure-DB

IMGT/3Dstructure-DB card

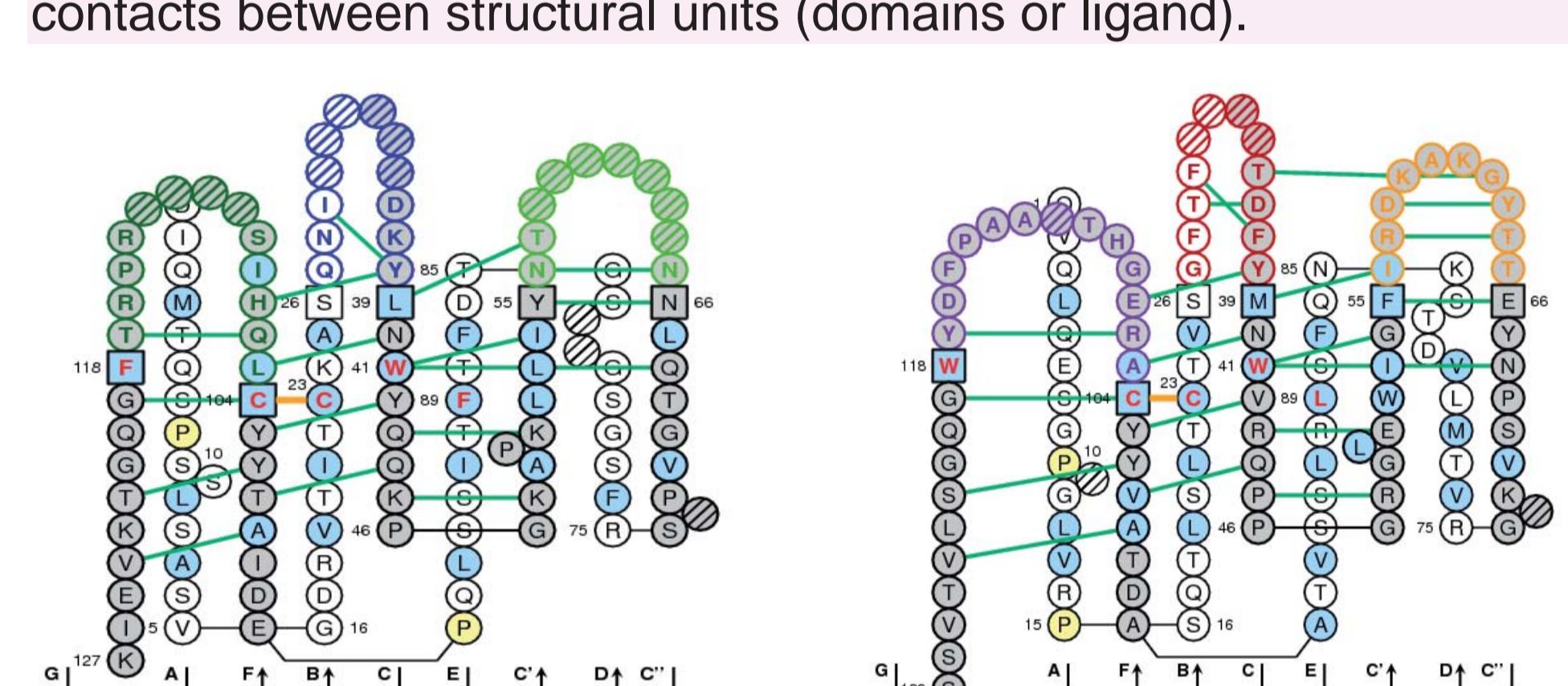
Chain details of CAMPATH-1H, alemtuzumab, MACCAMPATH-1, Ig, FAB-GAMMA-1_KAPPA Humanized (Humanized) [1ce1_H,1ce1_L]

Chain ID 1ce1_H
Chain length 220
IMGT chain VH-CH1
description = VH (1-121) [D1] + CH1 (122-219) [D2]
[1] QVLOESGPGLVRPSLTLCTVSGFTDFYMMWVPPGRIGLEIIFDIFRKAGKTYTEYNPSIKRVTILVDTSKNQFLRLSSVTVADATAYVYC
OH (1-22-219) [D2]
IN-AND-DI J-REGION 11
ADATAYVYCAGNEHATPFDWQQLGVVSSASTKGPSVFLAPSKSTGTAALGCLWDYFPEPVTVWSNSGALTSGVHTFPAVLQSSGLYSLSSVTVADATAYVYC
NT...
SGLSYLSVSVTVPSLSSGQTYQVNNKPSVTKVVKVE
Sequence in FASTA format Sequence in IMGT format

V-DOMAIN
IMGT domain description VH (1-121)[D1]
IMGT gene and allele name IGHV4-59*01 (93.0% Human), IGHV4*02 (92.90% Human), IGHV4*03 (92.90% Human)
IMGT gene and allele name IGHV4-59*01 (92.90% Human), IGHV4*02 (92.90% Human), IGHV4*03 (92.90% Human)
Alignment details
2D representation IMGT Collier de Perles or IMGT Collier de Perles on 2 layers
Contact analysis Domains contacts (overview)
CDR-IMGT lengths [8,10,12]
Sheet composition [A B D E F G] [C D R 1] [C D R 2]
QVLOESGP GLV PS ITSLCTVSGFTDFYMMWVPPGRIGLEIIFDIFRKAGKTYTEYNPSIKRVTILVDTSKNQFLRLSSVTVADATAYVYC
NT...
LSSATMDATAYVYCAGNEHATPFDWQQLGVVSSASTKGPSVFLAPSKSTGTAALGCLWDYFPEPVTVWSNSGALTSGVHTFPAVLQSSGLYSLSSVTVADATAYVYC
IGM7/DomainGapAlign results

If one 3D structure is available (for example 1ce1 for alemtuzumab), it is possible to query IMGT/3Dstructure-DB:

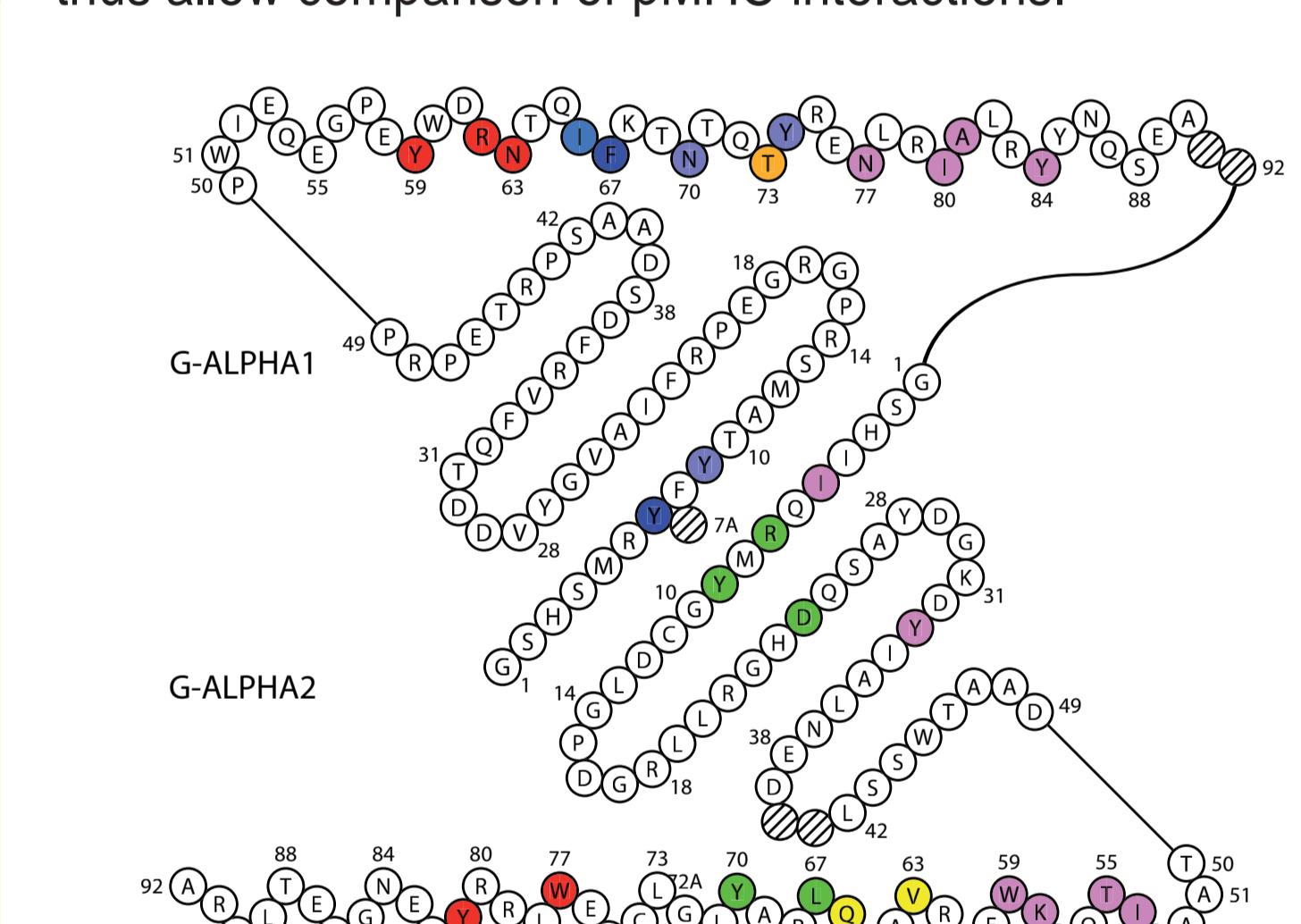
- to visualize hydrogen bounds in the IMGT Collier de Perles on two layers
- to check the contact analysis table. This table provides contacts between structural units (domains or ligand).



Contacts of 1ce1_H

Order	Port	Residue	Domain	Chain	Order	Port	Residue	Domain	Chain	Total	Polar	Hydrogen
<i>List of the Residue/Position pair contacts: Click 'XRF' for IMGT Residue/Position pairs</i>												
1	TYR	Y	VH	1ce1_H	2	THR	T	1ce1_P	I	4	0	0
2	TYR	Y	VH	1ce1_H	3	ALA	A	1ce1_P	I	13	1	0
3	TYR	Y	VH	1ce1_H	4	ASP	D	1ce1_P	I	14	2	2
4	PHE	F	VH	1ce1_H	5	SER	S	1ce1_P	I	5	0	0
5	PHE	F	VH	1ce1_H	6	SER	S	1ce1_P	I	16	0	0
6	PHE	F	VH	1ce1_H	7	ALA	A	1ce1_P	I	1	0	0
7	ARG	R	VH	1ce1_H	8	ASP	D	1ce1_P	I	9	3	2
8	ARG	R	VH	1ce1_H	9	ALA	A	1ce1_P	I	20	6	1
9	LYS	K	VH	1ce1_H	10	ASP	D	1ce1_P	I	11	2	1
10	GLU	E	VH	1ce1_H	11	ALA	A	1ce1_P	I	1	0	0
11	GLU	E	VH	1ce1_H	12	THR	T	1ce1_P	I	13	2	1
12	GLU	E	VH	1ce1_H	13	SER	S	1ce1_P	I	5	2	0
13	GLU	E	VH	1ce1_H	14	ALA	A	1ce1_P	I	5	0	0
14	GLY	G	VH	1ce1_H	15	GLY	G	1ce1_P	I	2	1	0
15	GLY	G	VH	1ce1_H	16	THR	T	1ce1_P	I	9	2	0
16	GLY	G	VH	1ce1_H	17	GLY	G	1ce1_P	I	24	4	0
17	GLY	G	VH	1ce1_H	18	THR	T	1ce1_P	I	21	5	0
18	GLY	G	VH	1ce1_H	19	ALA	A	1ce1_P	I	9	2	1
19	ALA	A	VH	1ce1_H	20	ALA	A	1ce1_P	I	1	1	0
20	ALA	A	VH	1ce1_H	21	SER	S	1ce1_P	I	11	4	1
21	ALA	A	VH	1ce1_H	22	SER	S	1ce1_P	I	3	1	0
22	ALA	A	VH	1ce1_H	23	THR	T	1ce1_P	I	3	0	0
23	ALA	A	VH	1ce1_H	24	THRE	T	1ce1_P	I	7	2	0
24	ALA	A	VH	1ce1_H	25	SER	S	1ce1_P	I	4	0	0
25	PRO	P	VH	1ce1_H	26	ALA	A	1ce1_P	I	5	0	0

IMGT pMHC contact sites graphically represent, in IMGT Colliers de Perles, the MHC amino acid positions that contact the peptide side chains in pMHC complexes, and thus allow comparison of pMHC interactions.



Ehrenmann F, Kaas Q. and Lefranc M.-P. Nucleic Acids Res. 38: D301-307 (2010)

IMGT/Collier-de-Perles

Make your own IMGT Collier de Perles

Domain type Variable (V)
Number of layers 1
CDR-IMGT color type 2 (IGK,IGL,TRA,TRG)
Background color IGM 80% chemical classes
Domain sequence DIOPTQSPSLASIGKPRVTTKASQNL...DKYLNWYQOKPGKAKPLLL...RPRPTFGQGTKEIK
Amino acid insertions Position Length Numbering labels ADD!
CDR-IMGT length 9
Your domain title
Draw!

Using the IMGT/Collier-de-Perles tool, IMGT Colliers de Perles can be displayed:

- on one or two layers
- with the VH or VL coloring of the CDR-IMGT
- with the IMGT amino acid physicochemical classes for the FR-IMGT. This allows to evaluate the number of IMGT amino acid class changes.

Pommie C. et al. J. Mol. Recognit. 17:17-32 (2004)

FR-IMGT and antibody humanization

A standardized comparison of V domain sequences for antibody humanization includes the delimitation of the FR-IMGT and CDR-IMGT, the determination of the CDR-IMGT lengths (e.g. [8.8.13]), the percentage of identity between FR-IMGT [calculated on 91 amino acids for VH (FR1-, FR2-, FR3-, FR4-IMGT: 25, 17, 38, 11) and 89 for V-KAPPA (FR1-, FR2-, FR3-, FR4-IMGT: 26, 17, 36, 10)] and the number of IMGT amino acid physicochemical class changes.

Humanized antibodies used in oncology

Humanized antibody	CDR-IMGT antibody	Closest Homo sapiens gene and allele	FR-IMGT identity	AA with IMGT class change in FR-IMGT
alemtuzumab	[8.10.12]	IGHV4-59*01	84.61% (77/91)	14
bevacizumab	[8.8.16]	IGHV7-4-1*02	74.72% (68/91)	24
trastuzumab	[8.8.13]	IGHV3-66*01	90.10% (82/91)	9
alemtuzumab	[6.3.9]	IGKV1-33*01	97.75% (87/89)	2
bevacizumab	[6.3.9]	IGKV1-33*01	92.13% (82/89)	7
trastuzumab	[6.3.9]	IGKV1-39*01	93.25% (83/89)	5

Note that the use of the IMGT unique numbering would enable to reach 100% for the FR-IMGT identity. Although a few positions need to be checked for antibody humanization such as 39 and 40 (FR2-IMGT) as they interact with CDR2-IMGT and CDR3-IMGT, respectively.

Magdelaine-Beuzelin C. et al. Crit. Rev. Oncol. Hematol. 64:210-225 (2007)

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